

Chapter 6

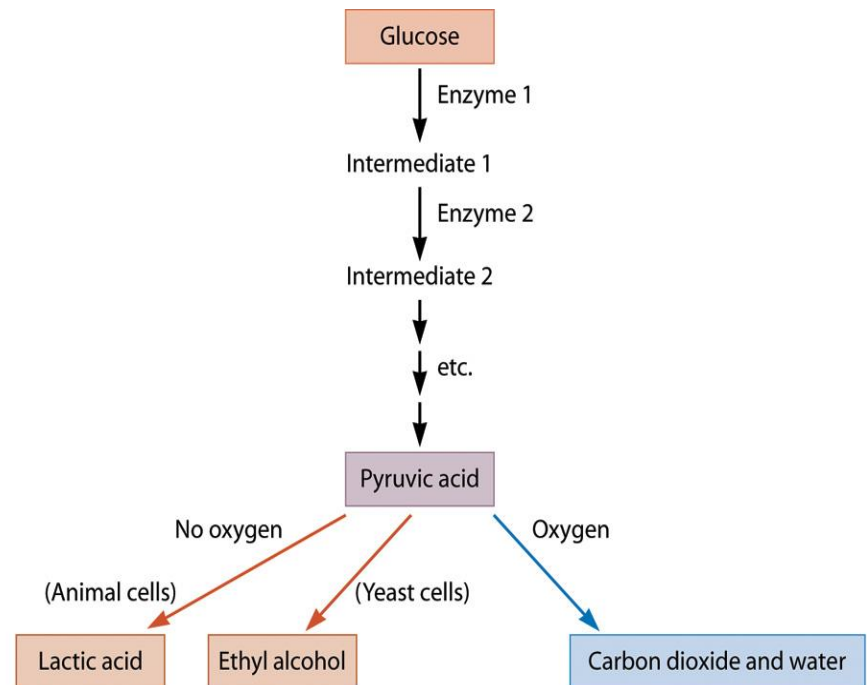
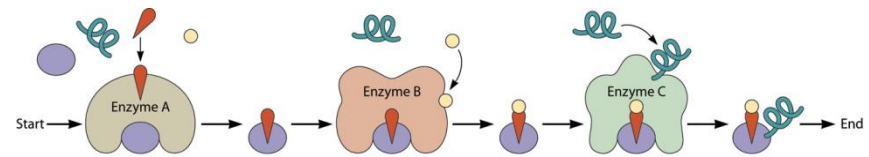
# Cell Metabolism



# Metabolic Pathways

## ■ Metabolic Pathways

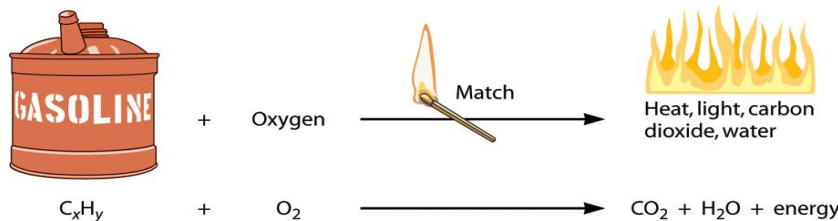
- Break down and manufacture molecules in a sequential set of reactions
- Enzyme reaction: generate products from substrates
- Networks of pathways : branch and converge
- Similar metabolic pathways from bacteria to human



# Catabolism and Anabolism

## ■ Catabolism

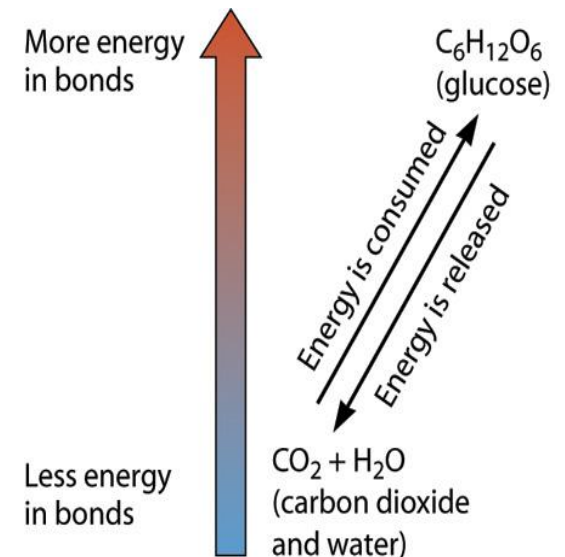
- Breaking down, Energy-yielding metabolism
- Energy release from bond breakage
  - Burning of gasoline
    - high E C-C, C-H bonds to lower E C-O, H-O bonds



- Burning of fat in human body
  - Enzymatic generation of molecules with lower E in bond

## ■ Anabolism

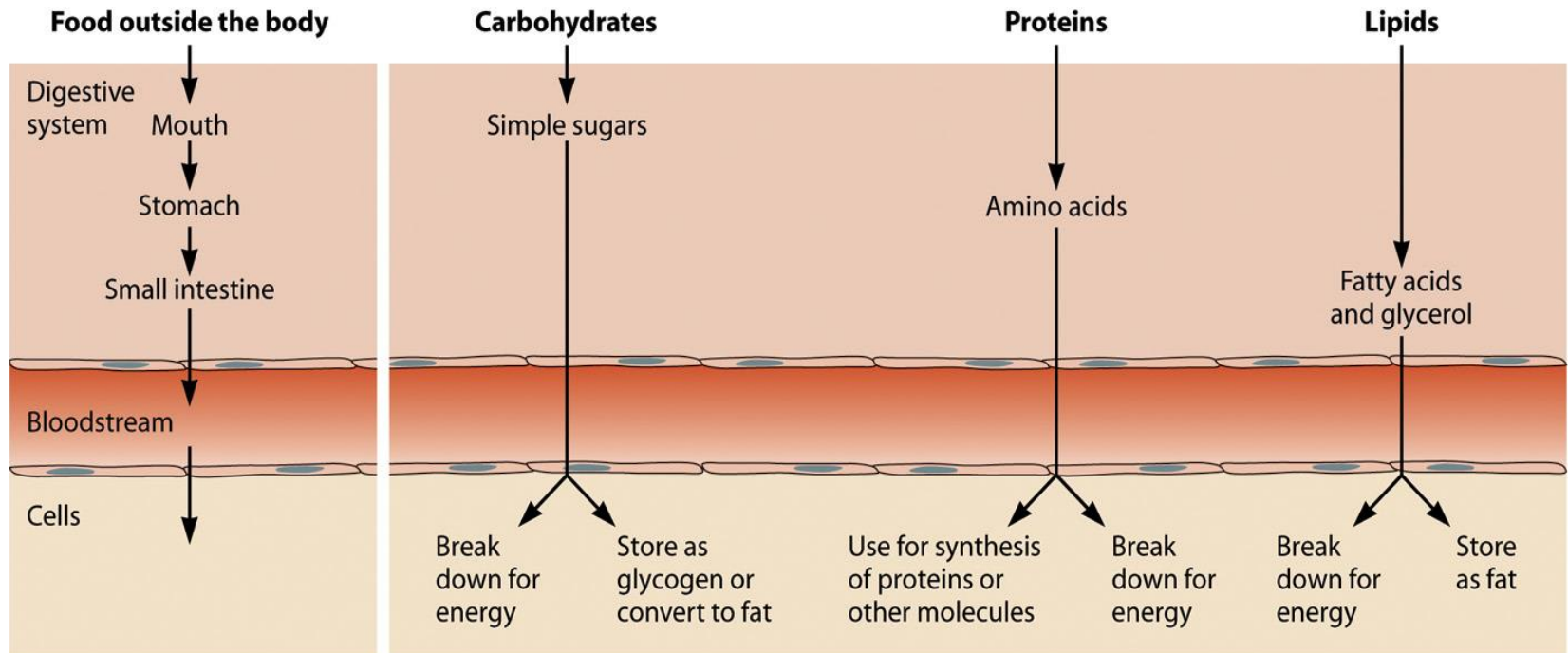
- Synthesis, Energy-requiring metabolism



# Catabolism of Food in Human Body

- Digestive system
  - Breaking down carbohydrates, lipids, and proteins into building blocks
  - Sugars
    - Used for quick E
    - If excess, stored as glycogen for short term storage (E for 1 to 2 days)
  - Fatty acids
    - Used for quick E
    - If not necessary, stored as fat (fat droplets in fat cells) for long term storage (E for 4-6 weeks)
  - Amino acids
    - Can be also used for E (but not the primary fate)
    - Used for protein synthesis and generation of other amino acids

# Catabolism in Animals



# Catabolism of Glucose

- Glycolysis
  - From bacteria to animals
  - Glucose (C<sub>6</sub>) to two pyruvic acid (C<sub>3</sub>)
  - No O<sub>2</sub> is required
- Aerobic conditions
  - Conversion of pyruvic acid to CO<sub>2</sub> and acetyl coenzyme A (acetyl-CoA)
  - TCA (Krebs cycle)
    - Acetyl CoA → CO<sub>2</sub> + H<sub>2</sub>O + NADH (temporary storage molecule)
- Anaerobic conditions
  - Fermentation
  - Generation of ethanol etc.

## BOX 6.1 *The exercise burn and a metabolic branch point*

Have you ever exercised until you felt your muscles burn? The burning is a direct result of a branch point in the metabolic pathway for breaking down glucose and other substrate molecules.

When you exercise, your muscles need a lot of energy. Exercising muscle cells break down lots of glucose—muscles even have their own glycogen stores for just such situations. Breaking down glucose to carbon dioxide and water requires another input: oxygen. When your muscles are working hard, you are breathing harder, and your heart is beating faster to supply your muscles with extra oxygen to power all that glucose catabolism. Sometimes, though, you cannot get enough oxygen to your muscles. You might be putting extraordinary demands on isolated muscles, as when you lift weights, or demanding output from your entire body that exceeds your capacity to supply oxygen via breathing and blood circulation, as when you sprint for a while.

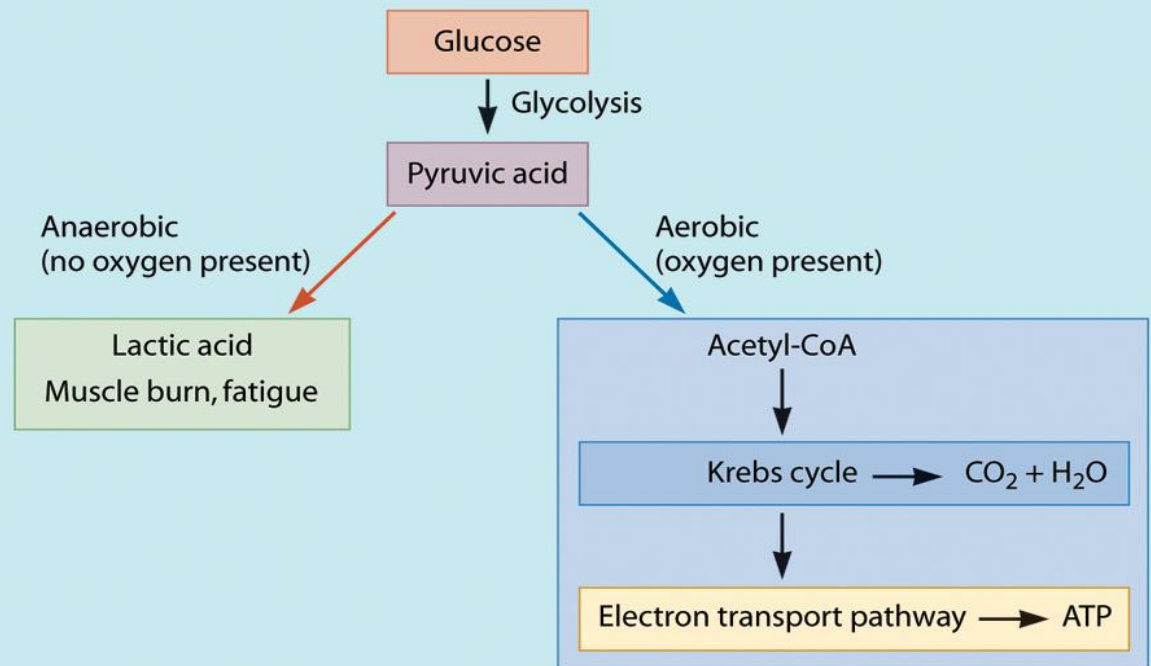
When your muscles can't get enough oxygen, the normal catabolism of glucose to carbon dioxide and water cannot happen. Look at the figure. When oxygen is present, pyruvic acid is converted into acetyl-CoA and on to carbon dioxide and water. This step is actually a

metabolic branch point. If oxygen is not present, your muscle cells do something different with the pyruvic acid. They have another enzyme that converts it into a three-carbon compound called lactic acid. When lactic acid builds up in your muscles, you feel that burning sensation.

The lactic acid burn is a sign that your muscles are working anaerobically (without oxygen). You've probably heard

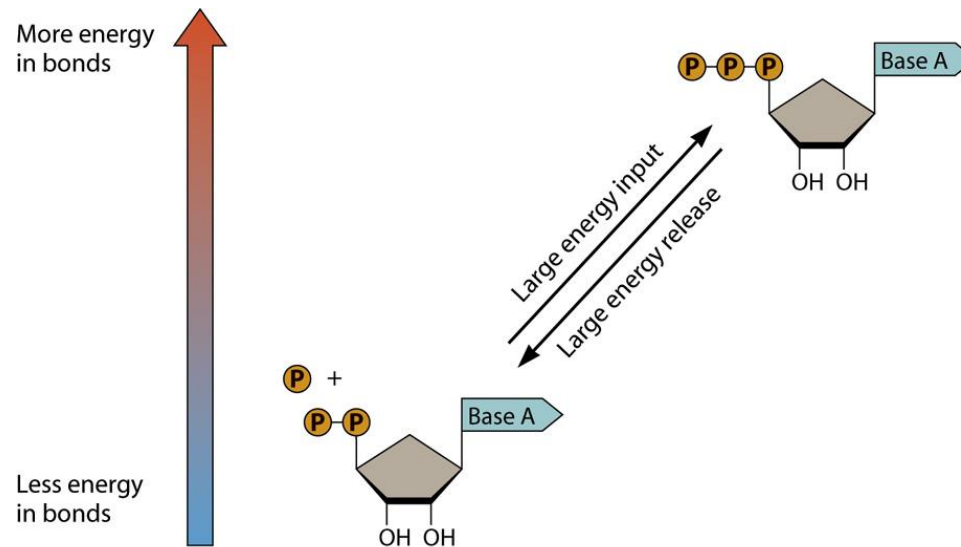
of aerobic exercise. The word aerobic means with oxygen. Aerobic exercise by definition causes you to breathe hard, but your breathing can keep up with your muscles' need for oxygen. That means you can sustain the exercise for longer periods of time. Because you are breathing harder and your heart is beating faster than usual during aerobic exercise, sustained exercise of this kind can strengthen your heart.

### Metabolism and muscle burn.



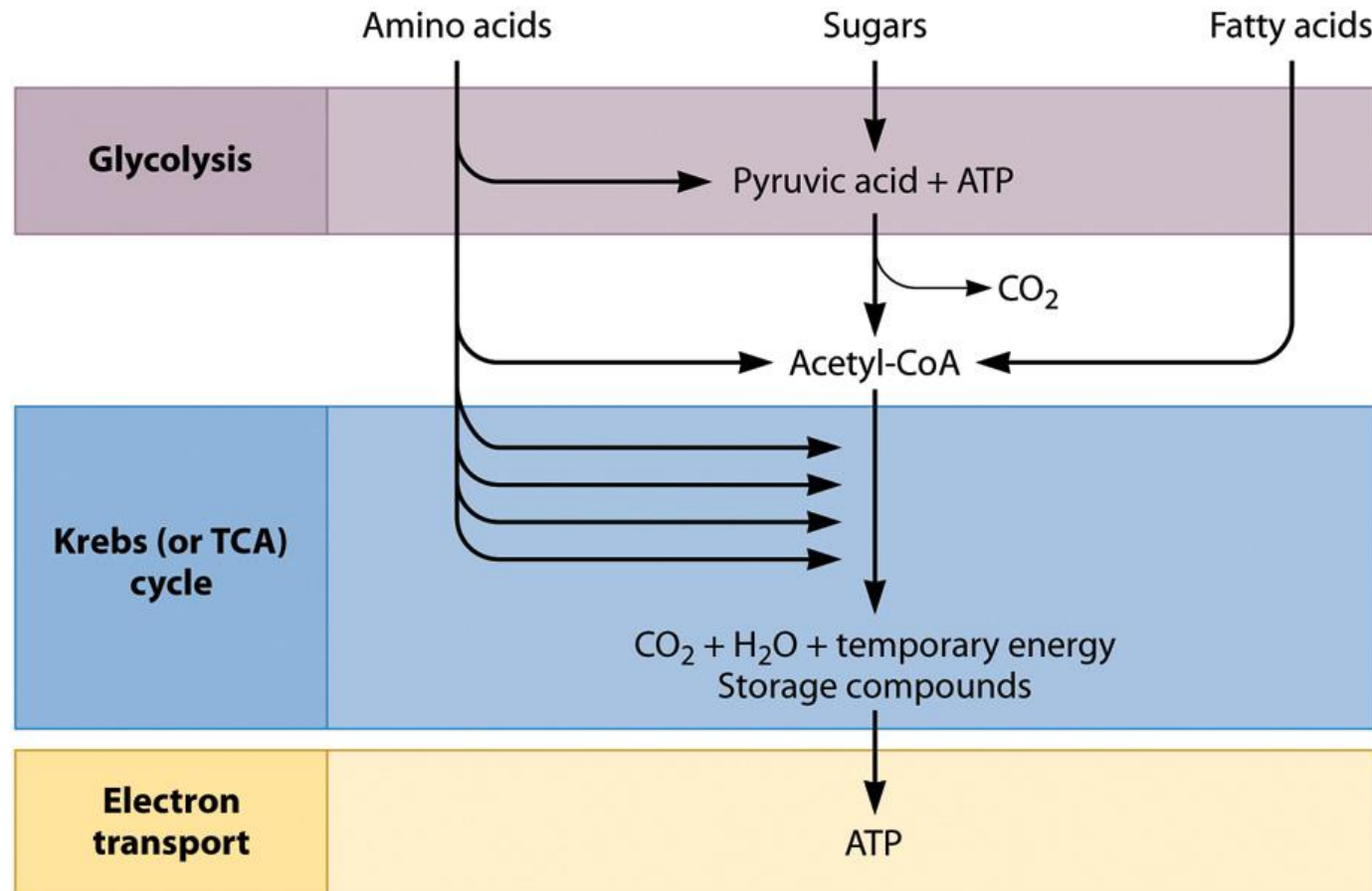
# Electron Transport Pathway

- Generation of ATP as E storage molecule
  - ATP : high E phosphodiester bond
- Reduction of  $O_2$  to  $H_2O$   
c.f. cyanide: blocking electron transport pathway



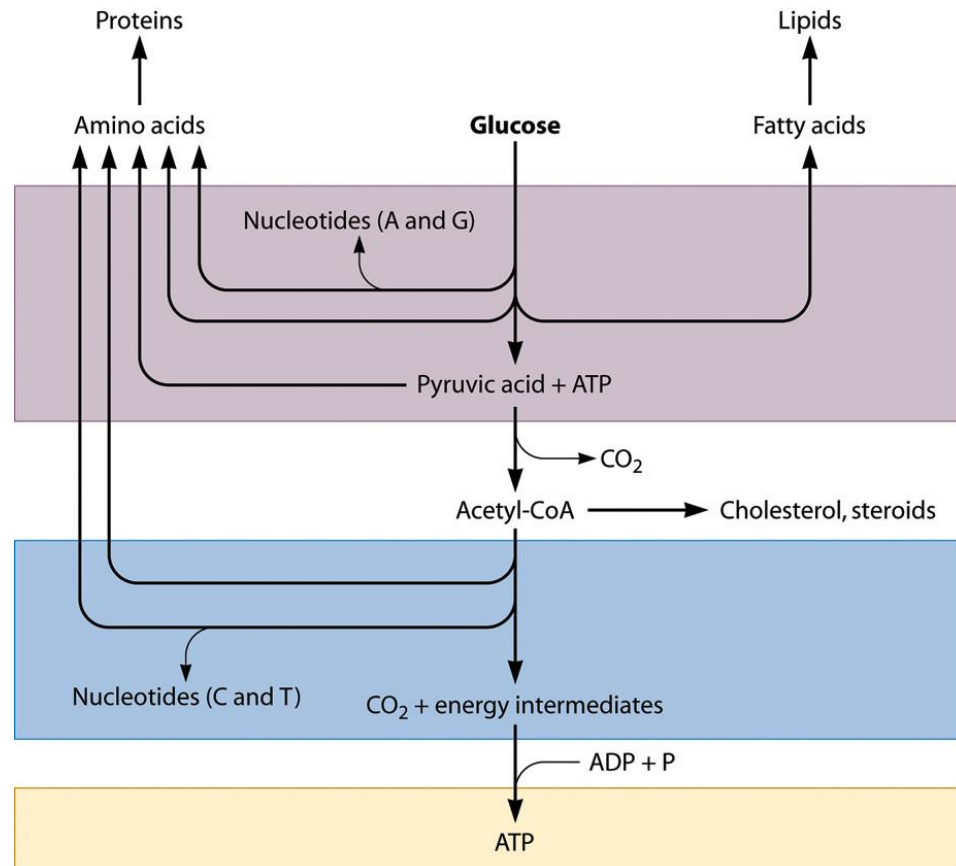


# Catabolism of Other Nutrient



# Anabolism

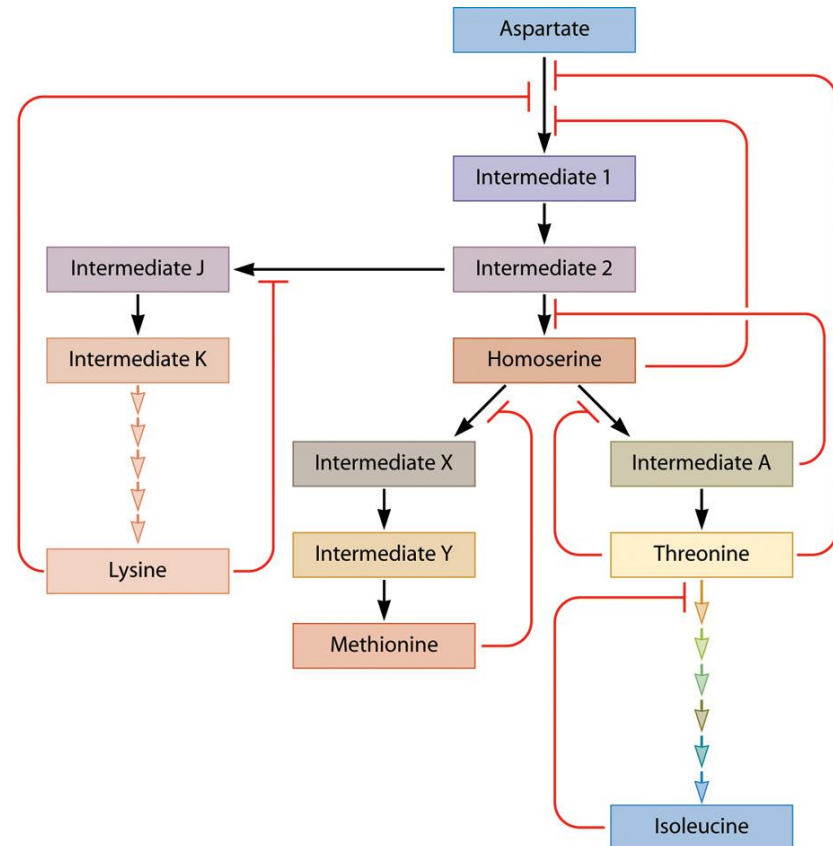
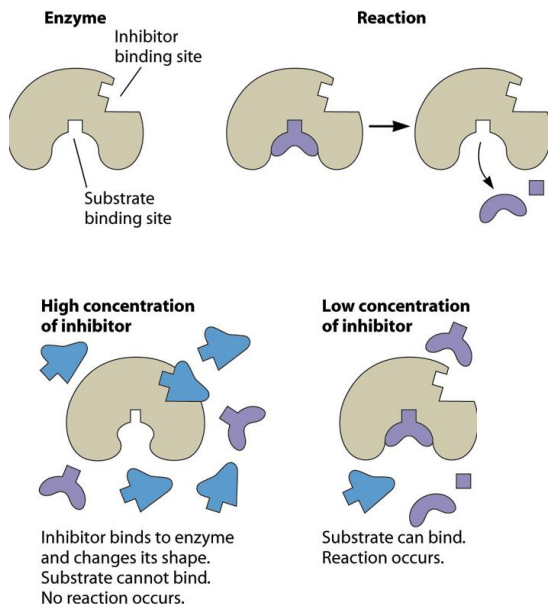
- Requirement
  - Energy: ATP
  - Chemical building blocks (intermediates of glucose breakdown)



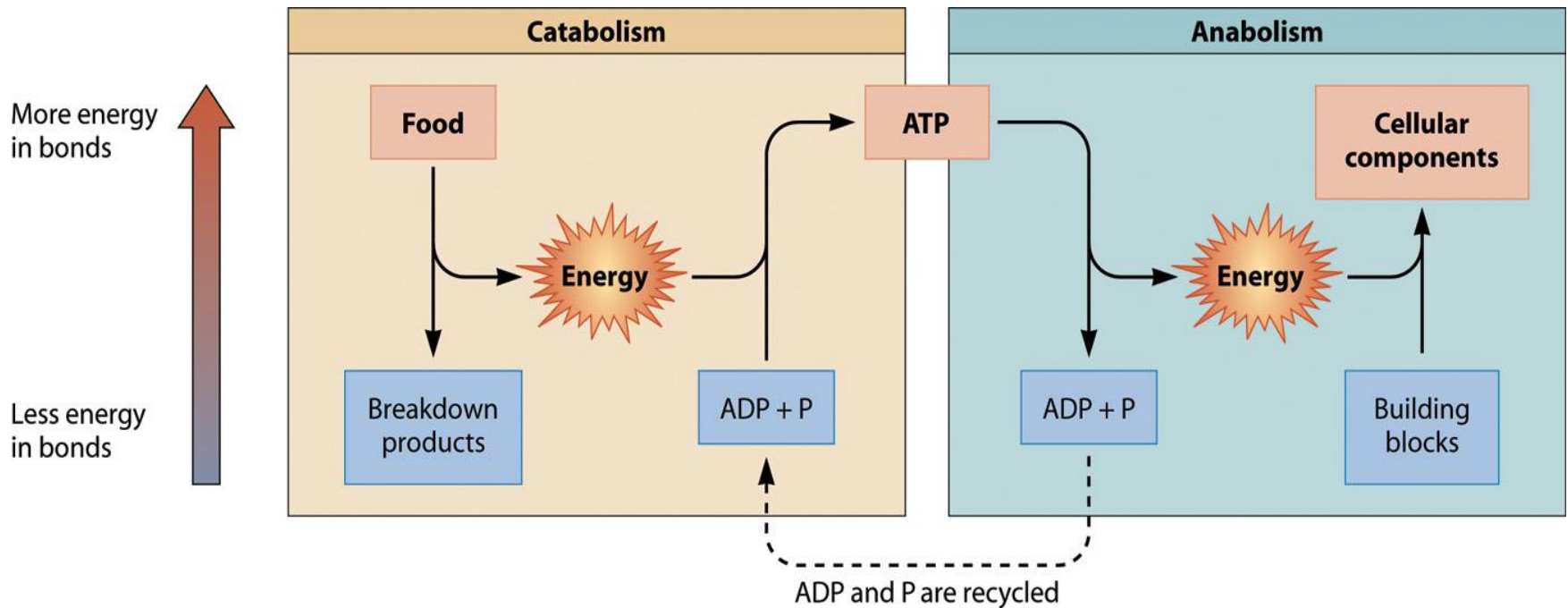
# Regulation of Metabolism

## ■ Feedback Inhibition

- Inhibition of enzyme activity by end product  
e.g. amino acid synthesis

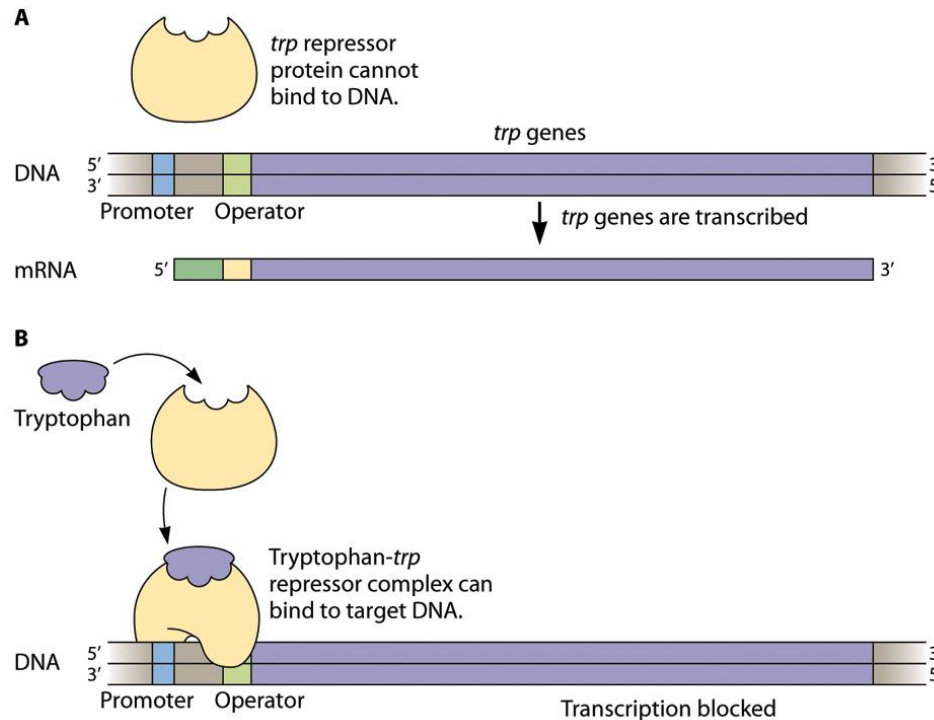


# Catabolism & Anabolism

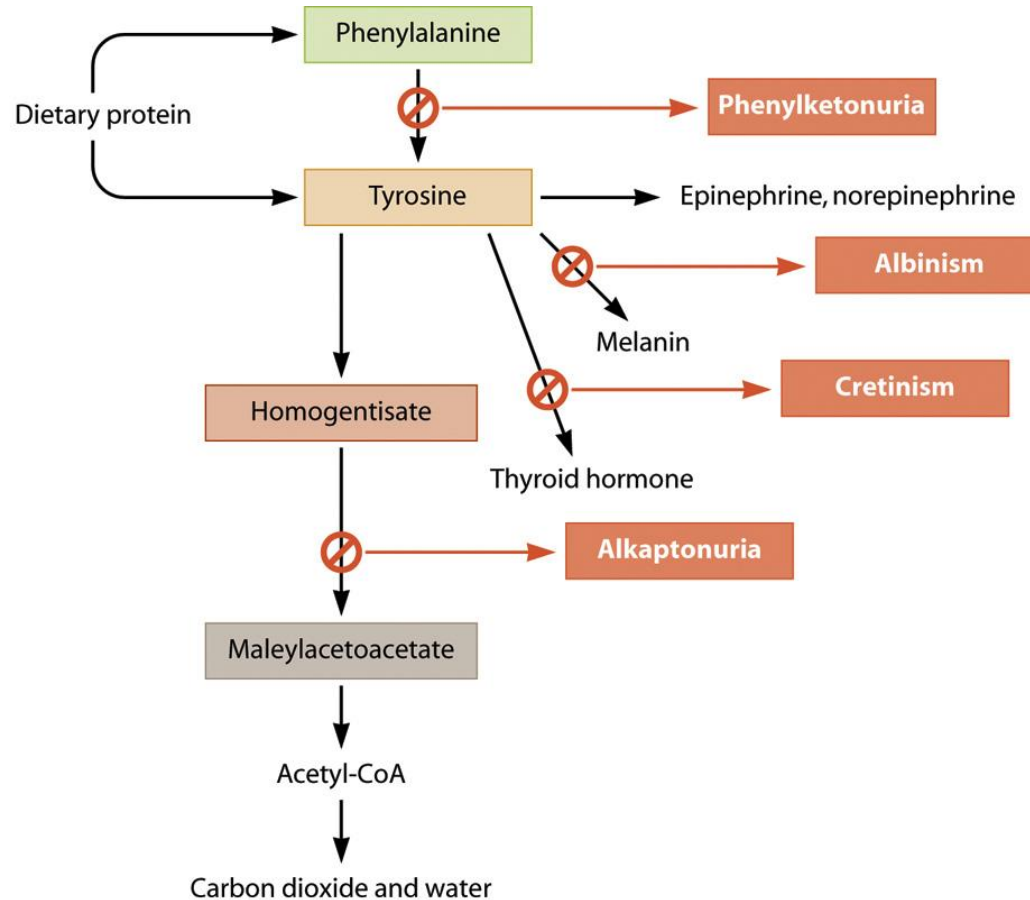


# Regulation of Metabolism by Gene Expression

- Trp synthesis in *E. coli*
  - Turn off transcription of Trp genes in the presence of Trp
- Hormonal regulation in higher eukaryotes



# Errors in Metabolism



# Errors in Metabolism

## ■ Enzyme defects and amino acid metabolism

### ■ Phenylketonuria (PKU)

- Phenylalanine hydroxylase (PAH) defect
  - No conversion of phenylalanine to tyrosine
  - Production of phenylketones
  - Excretion of phenylalanine and phenylketones in the urine
  - Phenylalanine inhibit normal development of nervous system
  - Treatment with controlled diet

Diet drink

--- warning

“Phenylketonurics: contains phenylalanine”

--- Aspartame(NutraSweet): Asp-Phe

### ■ Alkaptonuria

- Defect in enzyme converting homogentisate (HG) to maleylacetoacetate (MAA)
  - Oxidation of HG leads to black color → black urine
  - No serious effect

### ■ Albinism

- Lacking enzyme converting tyrosine to melanin

### ■ Cretinism

- Lacking enzyme converting tyrosine to thyroid hormone
- Defect in growth and maturation of the skeletal and nervous systems

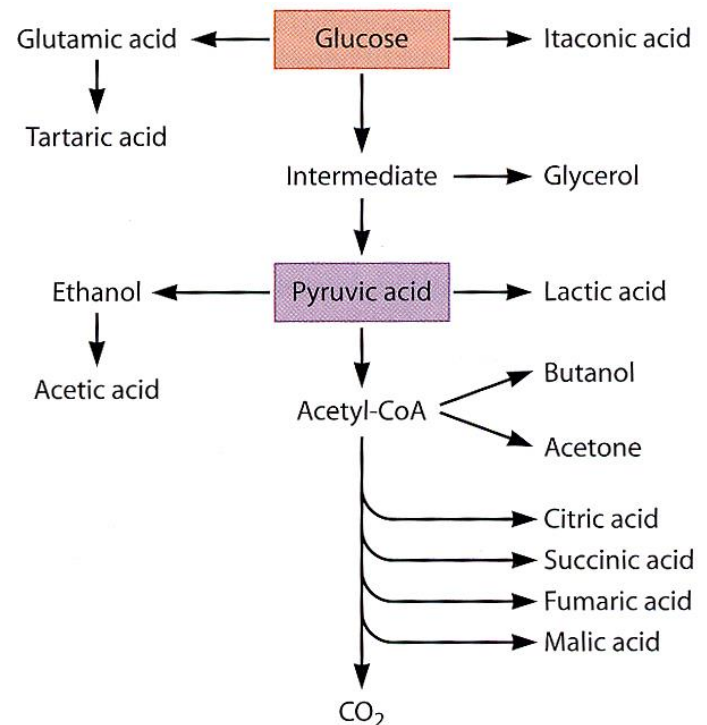
# Biotechnology Applications

- Treatment of Metabolic Disorders
- Gaucher's disease (pronounced go-shay)
  - Problems
    - Defect in enzyme breaking down glucocerebroside (lipid) in RBC and WBC
    - Accumulation of enlarged macrophage (Gaucher cell) in spleen, liver, and bone marrow
  - Treatments
    - Enzyme replacement of recombinant enzymes
    - Gene therapy



# Using Microbial Metabolism

- Using enzymes for manufacturing (Biocatalyst)
- Biotransformation
  - Whole cell reaction
    - e.g. production of fermented foods (wine, beer, cheese)
  - Reaction with isolated enzymes



# Generation of Useful Products from Microbial Metabolism

**Table 6.1** Chemicals currently produced by microbial metabolism of glucose and their industrial applications

| Chemical      | Microbial source                    | Industrial uses                                                                                |
|---------------|-------------------------------------|------------------------------------------------------------------------------------------------|
| Ethanol       | <i>Saccharomyces</i>                | Industrial solvent, fuel, beverages                                                            |
| Acetic acid   | <i>Acetobacter</i>                  | Industrial solvent, rubber, plastics, food acidulant <sup>a</sup> (vinegar)                    |
| Citric acid   | <i>Aspergillus</i>                  | Food, pharmaceuticals, cosmetics, detergents                                                   |
| Gluconic acid | <i>Aspergillus</i>                  | Pharmaceuticals, food, detergent                                                               |
| Glycerol      | <i>Saccharomyces</i>                | Solvent, cosmetic preparations, soaps, antifreezes                                             |
| Isopropanol   | <i>Clostridium</i>                  | Industrial solvent, cosmetic preparations, antifreeze, inks                                    |
| Acetone       | <i>Clostridium</i>                  | Industrial solvent, intermediate in many chemical synthesis reactions                          |
| Lactic acid   | <i>Lactobacillus, Streptococcus</i> | Food acidulant, fruit juice, soft drinks, dyeing, leather treatment, pharmaceuticals, plastics |
| Butanol       | <i>Clostridium</i>                  | Industrial solvent, intermediate in many chemical synthesis reactions                          |
| Fumaric acid  | <i>Rhizopus</i>                     | Intermediate in synthesis of synthetic resins, dyeing, acidulant, antioxidant                  |
| Succinic acid | <i>Rhizopus</i>                     | Manufacture of lacquers, dyes, and esters for perfumes                                         |
| Malic acid    | <i>Aspergillus</i>                  | Perfumes                                                                                       |
| Tartaric acid | <i>Acetobacter</i>                  | Acidulant, tanning, commercial esters for lacquers, printing                                   |
| Itaconic acid | <i>Aspergillus</i>                  | Textiles, paper manufacture, paint                                                             |

<sup>a</sup>An acidulant is a substance added to food or beverages to lower pH and to impart a tart, acid taste.

**Table 6.2** Useful products from microbial metabolic pathways other than glucose metabolism

| Type of product  | Examples                                            | Applications                                                                |
|------------------|-----------------------------------------------------|-----------------------------------------------------------------------------|
| Amino acid       | Glutamic acid, phenylalanine, aspartic acid, lysine | Nutritional supplements, flavor enhancers, sweeteners                       |
| Carbohydrate     | Dextran, xanthan gum                                | Food emulsifiers and thickeners, oil recovery                               |
| Vitamin          | B <sub>12</sub> , riboflavin, $\beta$ -carotene     | Nutritional supplements, pigments                                           |
| Metabolic enzyme | Proteases, amylases, lipases                        | Detergents, sweeteners, brewing, cheese making, textiles, leather softening |
| Nucleotide       | Guanosine, inosine                                  | Flavor enhancers                                                            |

# Application of Microbial Metabolism

- Bioremediation
  - Using microbes to degrade pollutants
  - e.g. Oil-eating microbes
- Enzymes in manufacturing
  - Invertase: soft-centered chocolate
  - Cellulase: stone-washed jeans
  - Amylase: reduced-calorie beer
  - Lipase, proteinases : laundry detergents